

Figure 1

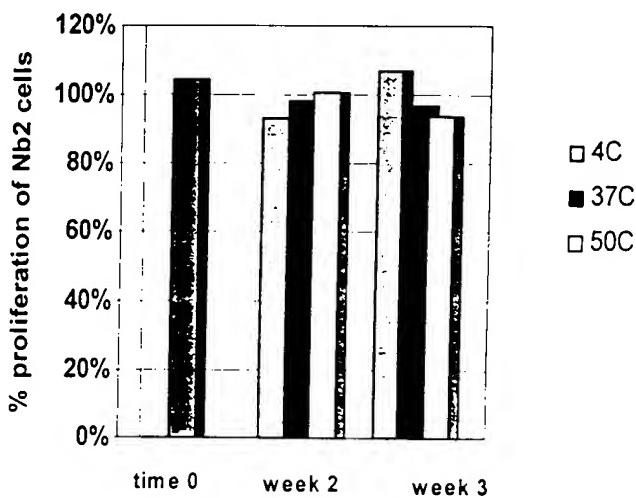


Figure 2

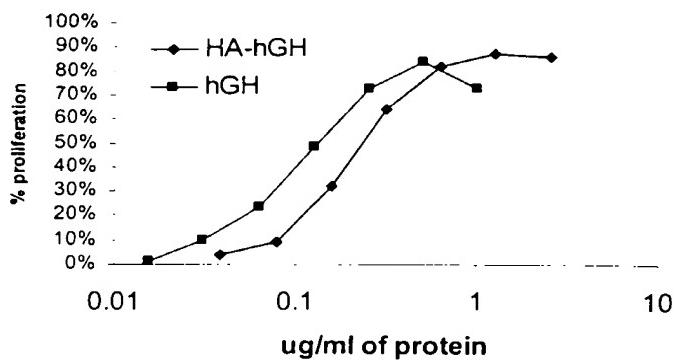


Figure 3A

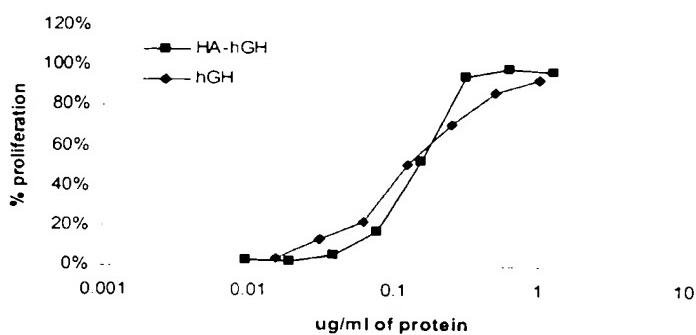


Figure 3B

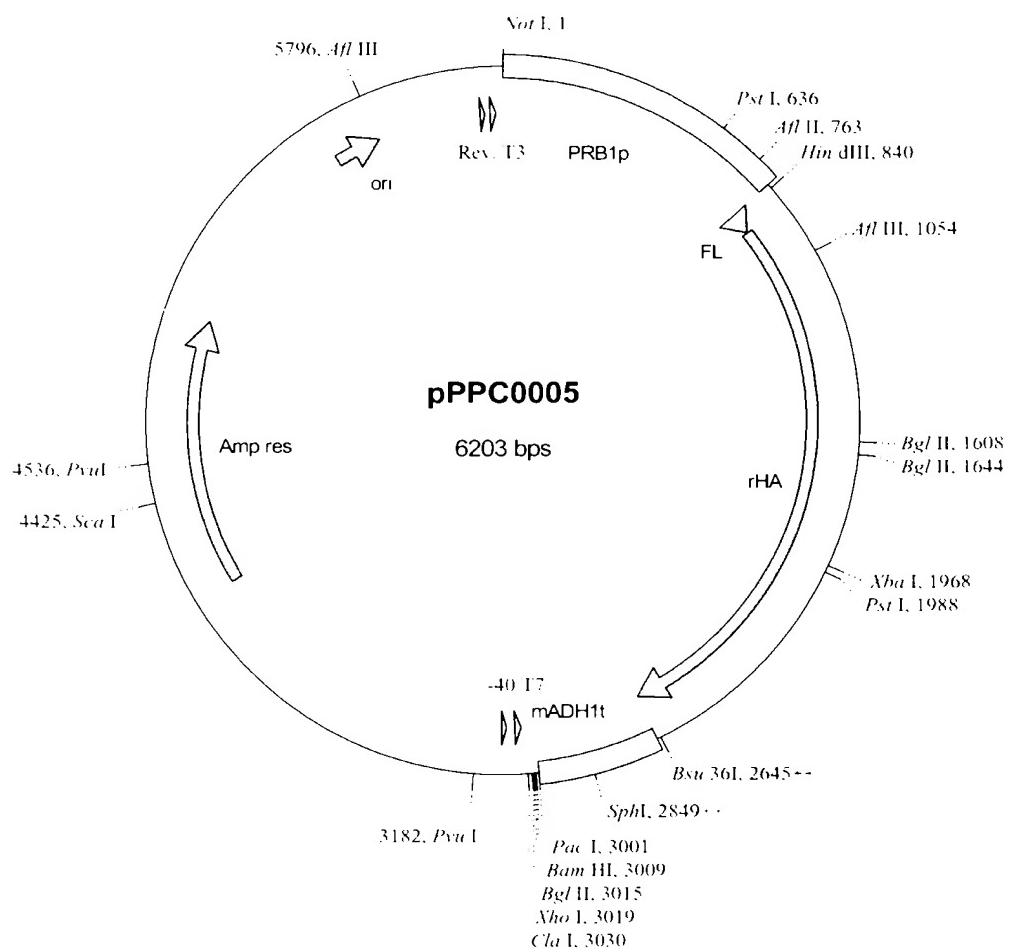


Figure 4

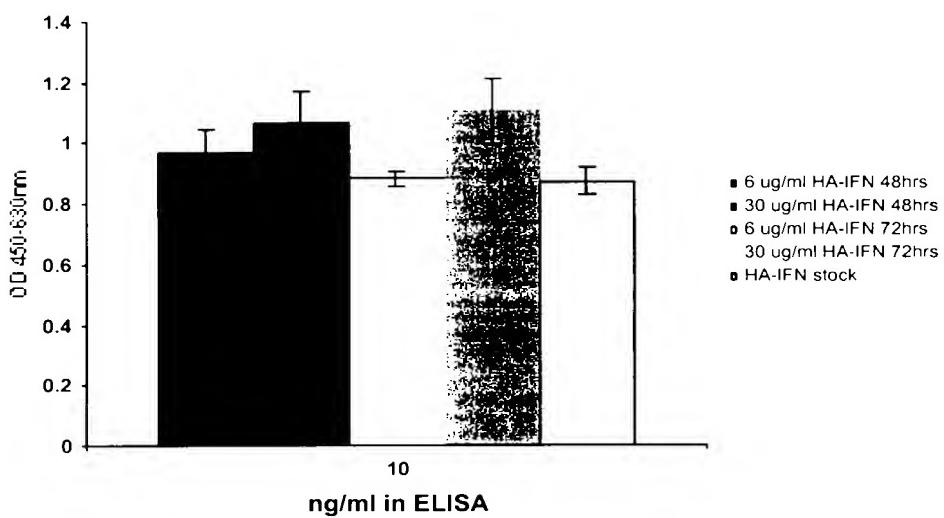


Figure 5

Figure 6

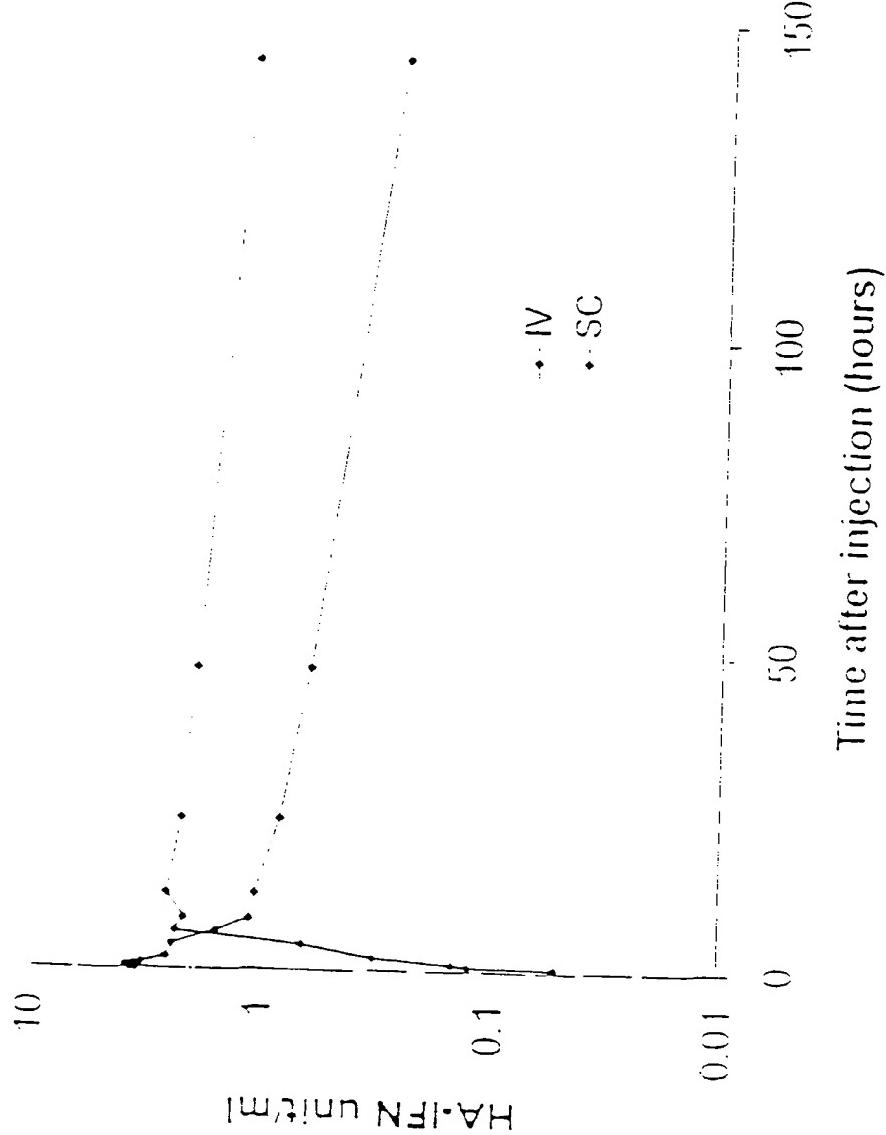
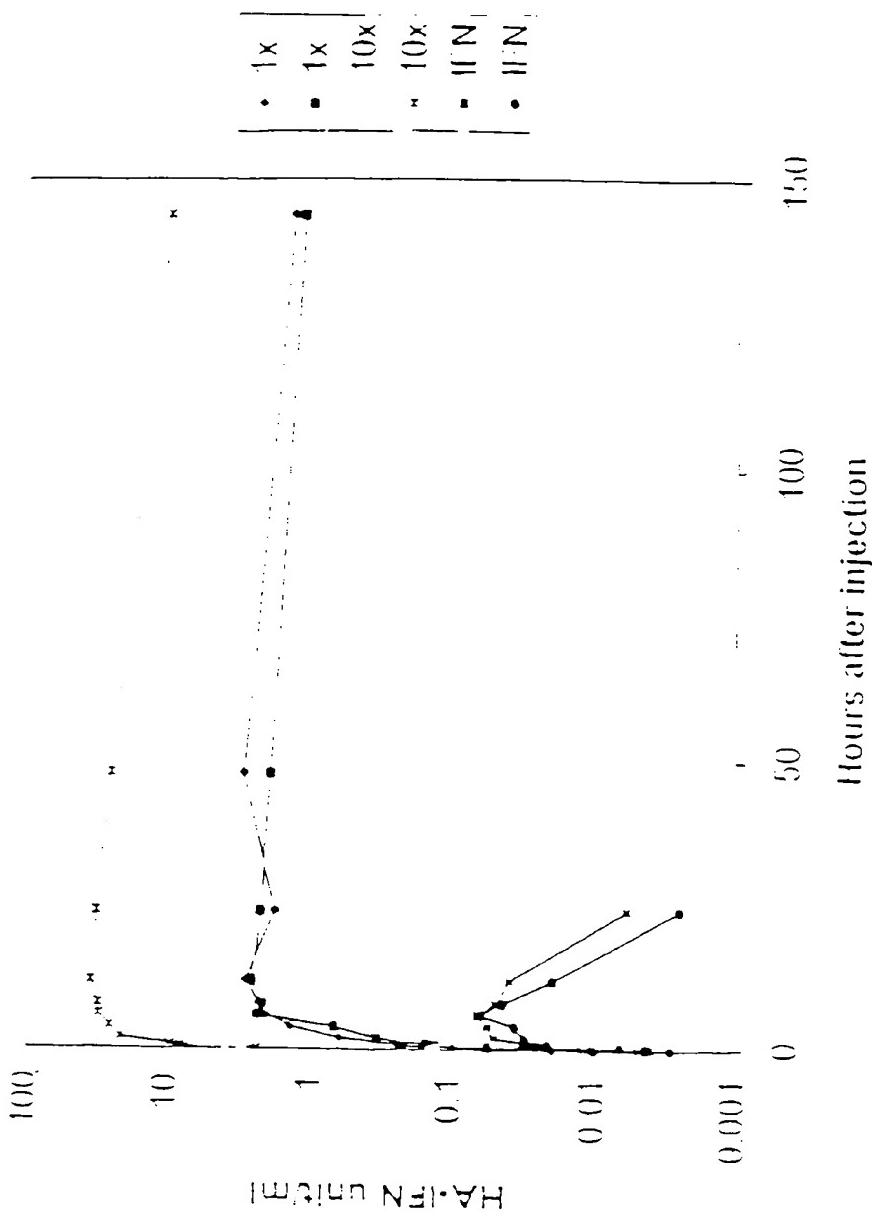


Figure 7



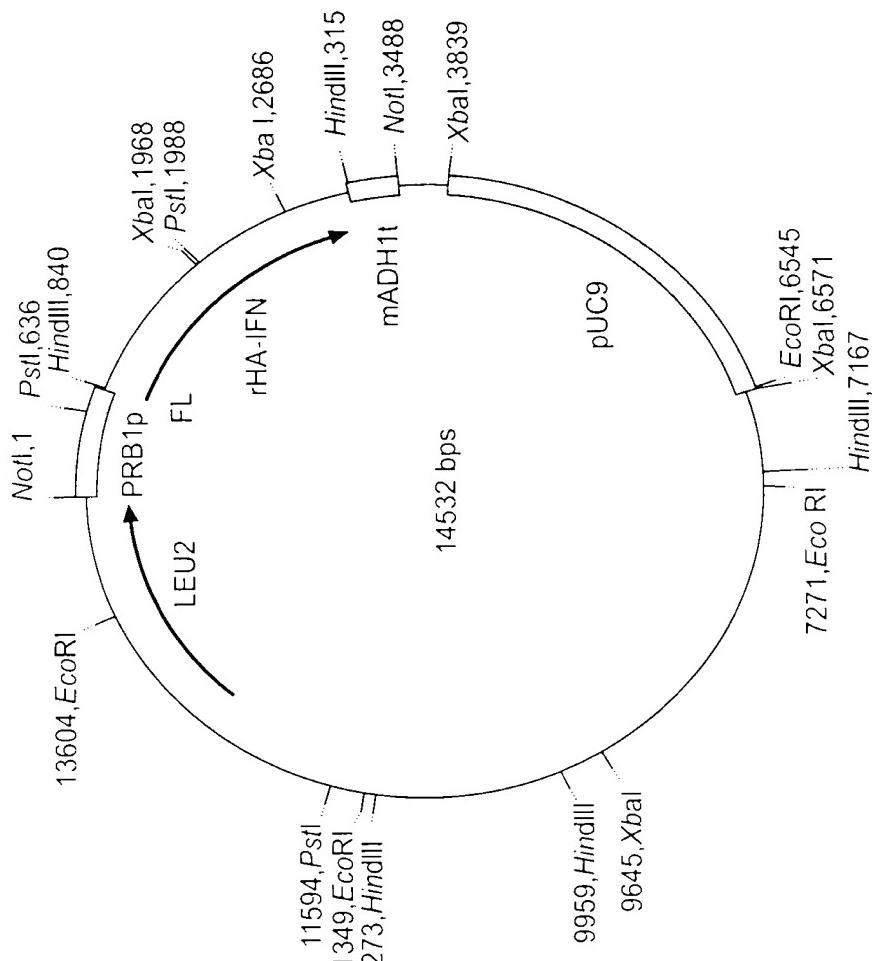


FIG. 8

Figure 9

Look

- I Val⁵⁴-Asn⁶¹
 II Thr⁷⁶-Asp⁸⁹
 III Ala⁹³-Glu¹⁰⁰
 IV Gln¹⁷⁰-Ala¹⁷⁷
 V His²⁴⁷-Cle²⁵⁵
 VI Cys²⁶⁶-Gln²⁷¹

Learn

- VIII Glu280-His288
 VIII Ala362-Glu368
 IX Lys439-Pro447
 X Val1462-Lys475
 XI Thr478-Pro486
 XII Lys484-Thr490

Figure 10

a. Randomisation of Loop IV.

IV

151 APPELLFFAKR YKAATTECCQ AADKAACLLP KLDELRDEGK ASSAKQRLKC
HHHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHHH HHHHHHHHHHHH

IV

151 APPELLFFAKR YKAATTECCX XXXXXXCLLP KLDELRDEGK ASSAKQRLKC
HHHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHHH HHHHHHHHHHHH

X represents the mutation of the natural amino acid to any other amino acid. One, more or all of the amino acids can be changed in this manner. This figure indicates all the residues have been changed.

b. Insertion (or replacement) of Randomised sequence into Loop IV.

(X),
↓
IV

151 APPELLFFAKR YKAATTECCQ AADKAACLLP KLDELRDEGK ASSAKQRLKC
HHHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHHH HHHHHHHHHHHH

The insertion can be at any point on the loop and a length where n would typically be 6, 8, 12, 20 or 25.

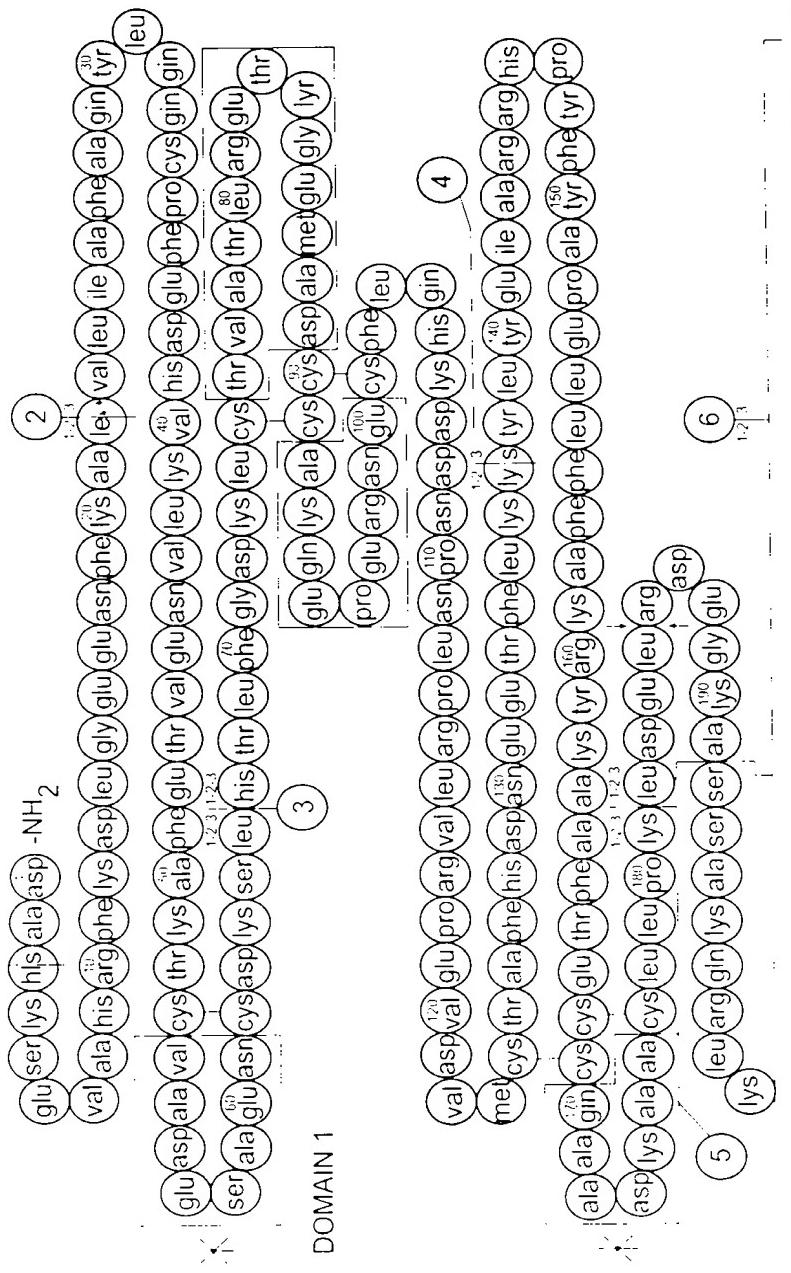


FIG. 11A

TO FIG. 11B

FROM FIG. 11A

FROM FIG. 11A

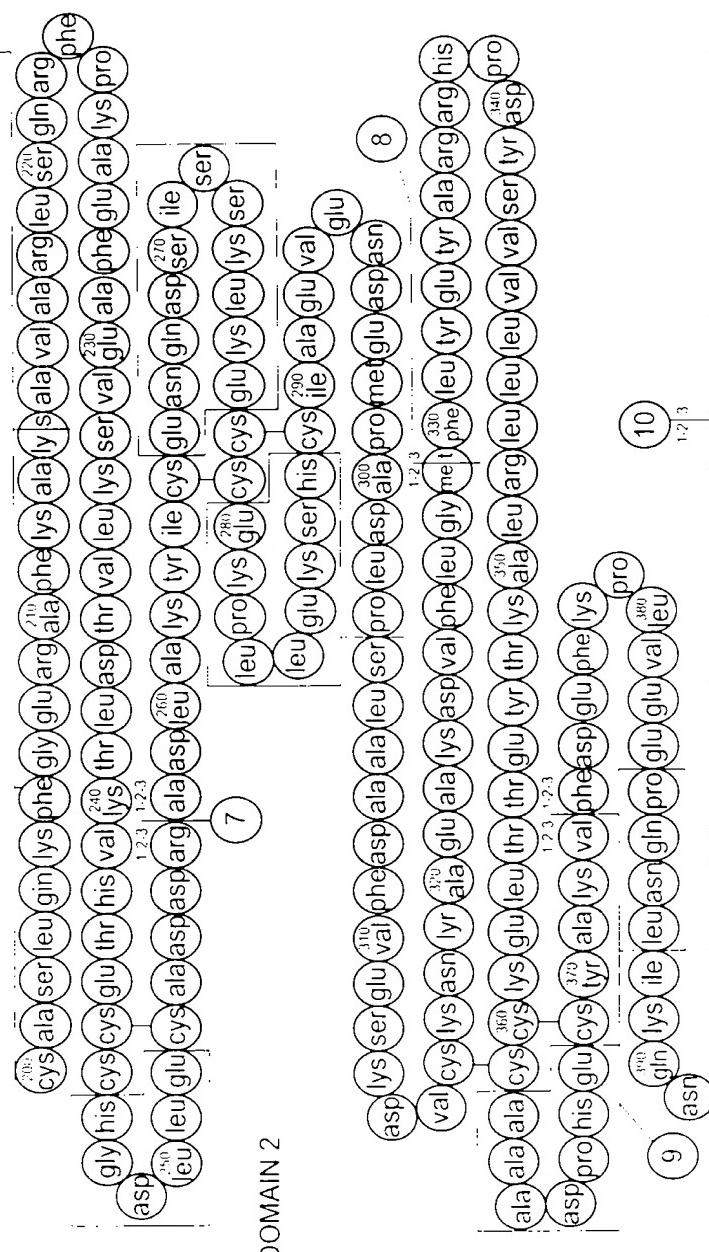


FIG 11C

TO FIG 11C

FIG. 11/B

FROM FIG. 11B

FROM FIG. 11B

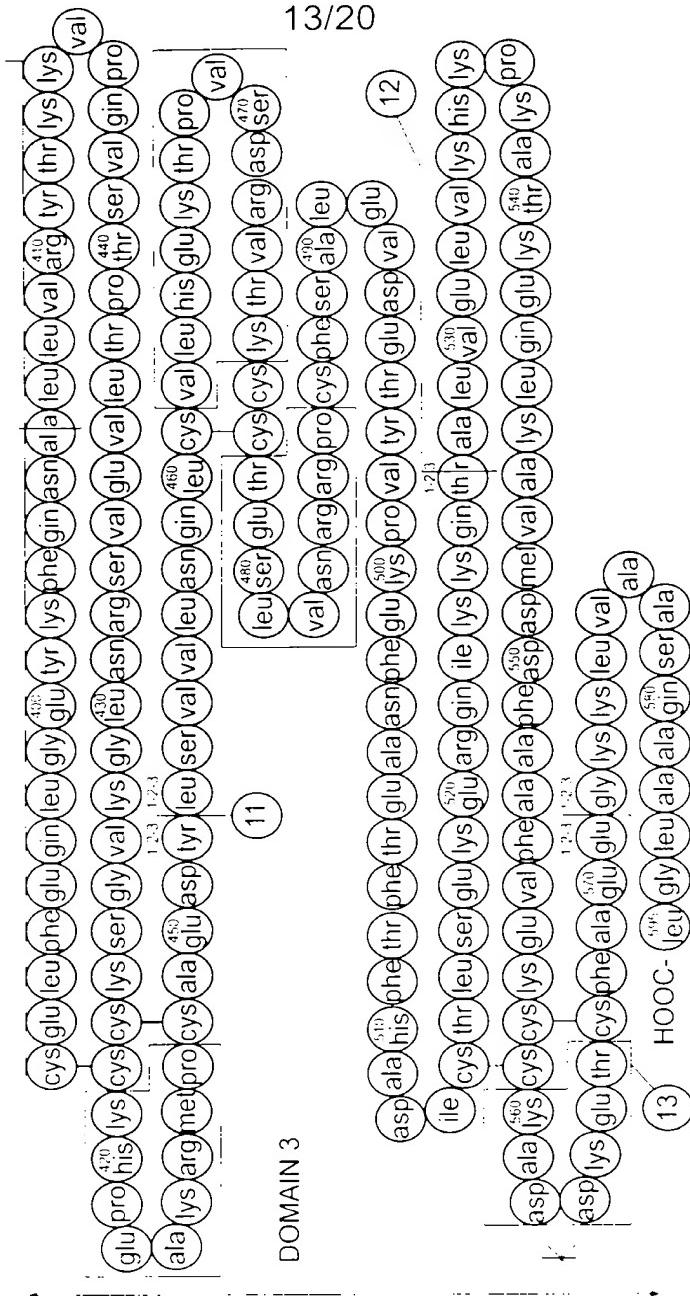


FIG. 11C

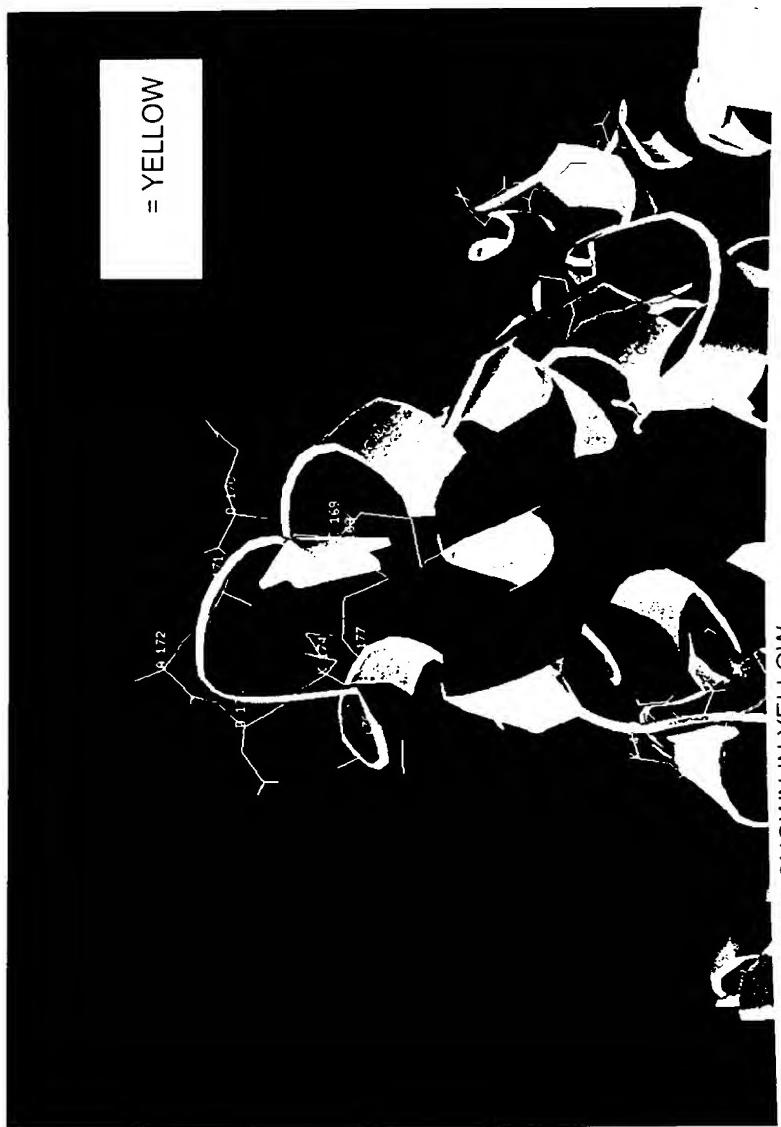


FIG. 12:
LOOP IV GLU170-A176

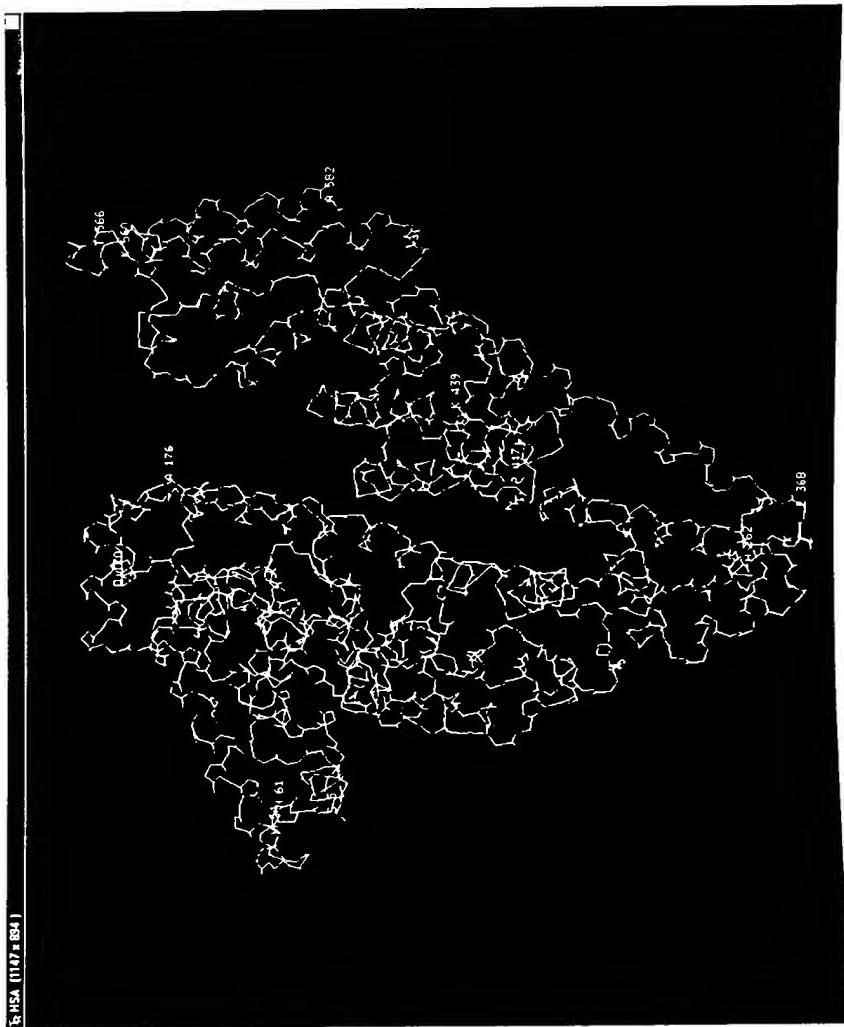


FIG. 13
TERTIARY STRUCTURE OF HA

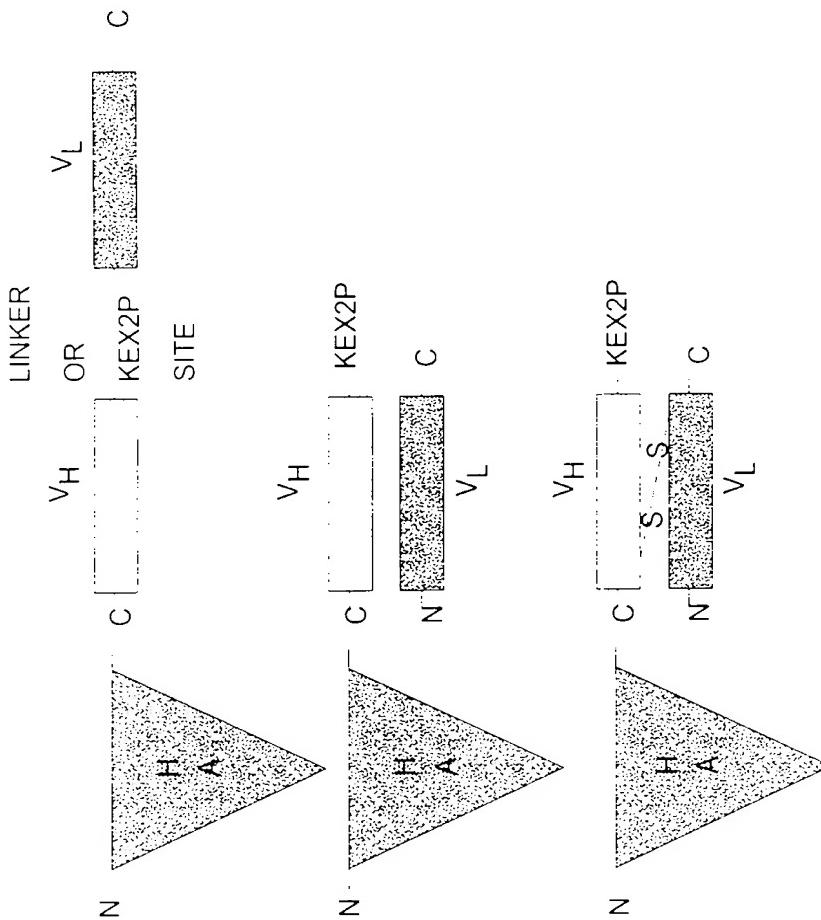


FIG. 14

Figure 15A

| | | | | | | | | | | | | | | | | | | | | |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|
| 161 | T | F | E | A | F | T | E | C | G | A | D | K | A | A | C | L | L | P | I | 180 |
| 162 | G | A | G | T | T | A | T | G | A | A | T | G | T | T | G | T | G | T | G | 600 |
| 163 | F | I | D | E | R | B | E | G | F | A | S | G | A | E | V | R | L | K | G | 200 |
| 164 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 400 |
| 165 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 600 |
| 166 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 600 |
| 167 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 600 |
| 168 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 600 |
| 169 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 600 |
| 170 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 600 |
| 171 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 600 |
| 172 | Q | R | F | P | H | A | E | F | A | E | F | A | E | F | A | Q | T | D | L | 720 |
| 173 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 174 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 175 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 176 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 177 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 178 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 179 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 180 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 181 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 182 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 183 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 184 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 185 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 186 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 187 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 188 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 189 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 190 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 191 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 192 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 193 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 194 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 195 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 196 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 197 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 198 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 199 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 200 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 201 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 202 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 203 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 204 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 205 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 206 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 207 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 208 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 209 | A | G | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |
| 210 | G | A | T | T | T | A | G | A | A | T | G | A | A | T | G | G | G | G | G | 720 |

Figure 15B

461 TAC AAA AGG GAT GTC TTT TGT TAA TAT GAA TAT TCA AAA AGG CAT CCT CAT 1020
471 E A K D V P L Q M F I Y E T A R R H P D 340

481 TAC TTT GTC ATT CTC CTC CTC RAA CCTT TCA RAA TAT GAA AAC ACT CTA GAG AAC TGC 1080
491 A A A A A A A A A K T Y E T P D E F K P L 360

1001 PCT TGT TTT TCA GAA CCTT TCA TAT GAA CCTT RAA TAT GAA TTT AAA CCTT CCTT CCTT 1140
1011 A A A A A A A A A K V A K V F P D E F K P L 380

1141 GTG GAA GAA CCT CTC RAA TAA AAC TTT GAA CCTT TTT GAG CG AG CCTT GGA GAG 1200
1151 V E E P D I I E E C H C E L F E Q L G E 400

1201 AAC RAA TTC RAA AGG GAT TGT TCA CCTT TCA TTT TCA CCC CAA GTA CCC CAA GTG TCA ATT 1260
1211 F F F F F F F F F F T K F Q P Q V S T 420

1261 TCA AGG TCA AGG GAT TGT TCA CCTT TCA TTT TCA CCC CAA GTA CCC CAA GTG TCA ATT 1320
1271 E E E E E E E E E E Q K V E S K C C K H 440

1321 CCT GAA TAA AAA RAA AAC CCTT GCA GAA GAC TAT CTA CCTG GTC CCTG AAC CAG TTA 1380
1331 F E K T P V S D R V L N Q L 460

1381 TAT TGT TTT CAT GAA AAA AGG CCA GCA RAA CCT CTC AGA GTC RAA AAA TGC TGC ACA GAG TCC 1440
1391 C V E H E K T P V S D R V L N Q L 480

Figure 15C

1441 TTG GTG AAC AUG CGA GAA GAA TAC TTT TCA CCT CTG GAA GTC GAT GAA ACA TAC GTT CCC AAA 1500
481 L V H R R P F S A L E V D E T Y V P K S 500

1501 GAG TTT ATT CCT GAA AGA TIC KCC TIC CAA GAT ATA TIC RNA CCT TCT TCT GAG AGG GAG 1560
481 E F H A E F P T F H A D I C T L S E K E 520

1561 ADA GAA GAA APV MKV NAK GAA ATC PAA CCT TCT TAG CCT TGT GAA CAC KAA CGG AAG GCA AGA 1620
481 R Q K F V P A G I E K L V K H P K A T 540

1621 ADA GAA 1680
481 K E Q L K A D P E F A A F V E K C K 560

1681 CCT GAC GAT AAA GAA GAA TAC TTT TAC GAT GAT TPC GAA GAA GAA GAA GAA GAA GAA GAA GAA 1740
481 A Q D K E I C F K H E G K K L V A S Q S 580

1741 CCT GTC TTA GAA 1782
481 A A S L 585

Figure 15D